University Investment in Drug Discovery

ALTHOUGH YOUR SPECIAL SECTION ON DRUG Discovery (29 July, pp. 721–735) highlighted important contributions from academia, it did not recognize an increasingly relevant but underappreciated and underutilized role for academic research in drug discovery.

Universities invest many millions in basic research that exposes disease mechanisms and therefore unearths new targets. Yet few have invested in the relatively modest infrastructure required to put their discoveries to the test. As a result, many promising targets gather dust on the university shelf. This need not be the case. Developing appropriate assays, screening modest-sized compound libraries, using medical chemistry to further develop leads, and conducting preliminary tests in animal models are functions well suited to academia. Academic researchers often have the best understanding of individual targets, routinely design and refine in vitro assays, and have ready access to and experience with the most appropriate animal models.

> "Universities invest many millions in basic research that exposes disease mechanisms… [y]et few have invested in the relatively modest infrastructure required to put their discoveries to the test."
>
> —IVINSON

The pharmaceutical industry (and, to a lesser extent, biotech) look at drug discovery ideas emanating from academic research as too risky and early in development to warrant significant investment. This risk aversion is in large part a reflection of the economic climate and the changing winds of drug-discovery received wisdom. To bring these ideas to a stage where pharma will look at them more carefully, we can and should advance them through at least the first stages of drug discovery. Demonstrating a credible mechanism and target, proprietary lead compounds, and preliminary in vivo efficacy will be enough to bring some of our industry colleagues back to the table. But this will only happen when academics stop treating drug discovery as the intellectually inferior domain of the commercial sector and start seeing it as the natural development of their research.

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A Place at the Pharma Table for Women?

THE ARTICLE "IT'S STILL A MAN'S WORLD AT THE top of big pharma research" (J. Mervis, Special Section on Drug Discovery, News, 29 July, p. 724) resonated with me. As a scientist in Merck R&D in the 1990s, it was clear to me that women did not have a place at the decision-making table. As years of diversity committees, on-site day care, mentoring programs, coaching, and other HR efforts rolled by, many talented women figured out that their only career path at Merck R&D was out the door.

Merck, and I suspect many other "big pharma" companies, are feeling the effects of having some of their best talent leaving and taking their brainpower elsewhere. We have started companies, taken senior positions in biotechnology firms, and become leaders in government and academia. Perhaps this brain drain of talented women has exacerbated the problem of the empty product pipelines of big pharma.

The men in charge of R&D tend to promote and recruit other men with whom they feel the most comfortable and ignore talented women. Until they are forced by progressive senior executives to include, in significant numbers, women in their club, they will not change.

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Costs and Benefits of Regulating Mercury

MERCURY IS KNOWN TO HAVE DETRIMENTAL effects on human health (*1*), so it is surprising to read that it may not be worthwhile to regulate mercury releases from U.S. power plants ("Regulating mercury: what's at stake?", T. Gayer, R. W. Hahn, Letters, 8 July, p. 244). Although there is legitimate debate about the cost of implementation and the choice of emission reduction approach, we feel that the estimated benefits of emission reduction of $100 million accrued over 15 years have been grossly understated by Gayer and Hahn.

Their proposed benefit was based on a study of willingness-to-pay for chelation therapy to reduce lead in children. However, lowering levels of lead by chelation has not been demonstrated to improve cognition (*2*). Similarly, although chelation therapy may remove methyl- and ethylmercury, it cannot reverse central nervous system damage (*3*), implying that prenatal mercury exposure leads to lifelong lost benefits, irrespective of money spent on removing the causal agent from the body after the damage has been done.

Thus, an approach based on lifelong losses in income better estimates the benefits of reducing mercury emissions (*4*). This approach attributes subsequent losses in lifelong earnings as a result of lower IQ to the loss in a child's IQ from prenatal methylmercury exposure. The estimated lifelong losses in income for all U.S. children affected in the year 2000 was $1.3 billion per year (range: $0.1 to $6.5 billion), which would lead to a $15.9-billion loss in income (range: $1.2 to $79.9 billion, discounted at a rate of 3% per annum) over the 15-year period considered by Gayer and Hahn. Therefore, by only considering the loss of earnings due to exposure to mercury generated by U.S. power plants, lowering prenatal exposure by reducing emissions may have considerable economic benefits, likely exceeding the estimated costs of $4 billion to $19 billion.

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References

1. P. Grandjean *et al.*, *Neurotoxicol. Teratol.* **19**, 417 (1997).
2. K. N. Dietrich *et al.*, *Pediatrics* **114**, 19 (2004).
3. X. Liu *et al.*, *Pediatrics* **110**, 787 (2002).
4. L. Trasande, P. J. Landrigan, C. Schechter, *Environ. Health Perspect.* **113**, 590 (2005).

Response

IN OUR STUDY, WE ESTIMATED THE COSTS and benefits of the U.S. Environmental Protection Agency's (EPA) power plant mercury regulation. To estimate the benefits of mercury reduction, we considered each link in the pathway, including the reduction of emissions from U.S. power plants; reductions in mercury deposition; reductions of methylmercury in U.S. freshwater and marine fish; reductions of methylmercury consumption from U.S. fish by U.S. resi-

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dents; reductions of methylmercury in U.S. women of childbearing age; and IQ improvements in U.S. children. For each link, we used the best available evidence and, if anything, tended to err on the side of overstating benefits. Only at the end did we monetize estimates of IQ improvements, based on a study of parental willingness to pay for IQ increases through chelation.

Zeller and Booth contend that our estimate of the benefits of mercury reduction is "grossly understated" based on their claim that our estimate of the value of an IQ point is flawed. They cite a study by Trasande *et al.* (*1*) claiming that benefits of mercury reduction are $1.3 billion per year. Unfortunately, they are comparing apples with oranges. The $1.3 billion estimate (*1*) is for the benefits of eliminating all U.S. power plant mercury emissions. Zeller and Booth apply this annual measure of complete elimination of power plant mercury emissions to each year from 2005 to 2020. It is incorrect to compare the costs of EPA's regulation that eliminates a fraction of the power plant emissions to the benefits of eliminating all power plant emissions of mercury (which would cost considerably more to achieve).

Zeller and Booth suggest that the monetized benefits we use for IQ may be understated. We agree that the willingness-to-pay numbers for IQ may understate the benefits of IQ. The value of an IQ point suggested by Trasande *et al.* (*1*) is about an order of magnitude greater than our estimate. However, as we noted in our Letter, using their estimate does not change our finding that the costs of the regulation are likely to exceed benefits.

Zeller and Booth's claim of mercury's detrimental effects might be overstated. They cite Grandjean *et al.*'s study (*2*) of the Faroe Islands to support their claim that the detrimental effects of mercury are "known." They do not mention a study of the Seychelles (*3*) that did not find evidence of such a link and a study in New Zealand (*4*) that found mixed evidence. Even Grandjean *et al.* (*2*) found mixed results for the relationship between mercury and IQ scores. Nonetheless, we used conservative estimates of the IQ-mercury relationship even when they are not statistically different from zero.

We think that policy-makers should design regulations for controlling mercury emissions so that expected benefits exceed expected costs. The current approach fails that test.

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References

1. L. Trasande, P. J. Landrigan, C. Schechter, *Environ. Health Perspect.* **113**, 590 (2005).
2. P. Grandjean *et al.*, *Neurotoxicol. Teratol.* **19**, 417 (1997).
3. G. J. Myers *et al.*, *Lancet* **361**, 1686 (2003).
4. T. Kjellstrom *et al.*, *Physical and Mental Development of Children with Prenatal Exposure to Mercury from Fish. Stage 2: Interviews and Psychological Tests at Age 6* (National Swedish Environmental Board, Solna, Sweden, 1989).

Landscape Corridors: Possible Dangers?

THE REPORT "EFFECTS OF LANDSCAPE CORRIDORS on seed dispersal by birds" (1 July, p. 146) by D. J. Levey *et al.* shows that landscape corridors increase the movement of birds between patches of habitat in a fragmented landscape, and that this facilitates the movement of bird-dispersed seeds. Another study, in the same experimental setting, found that corridors increase interpatch insect pollination (*1*). Both studies conclude by emphasizing the conservation value of habitat corridors. However, landscape corridors also facilitate the spread of invasive alien species (*2*). Although the potential negative effects of habitat connectivity were stated almost two decades ago (*3*), these seem to have been largely ignored in the evaluation of corridors as a conservation tool.

Alien plants with attractive flowers and fruit can hijack generalist pollinators and seed dispersers from indigenous plant species (*4*). By increasing alien propagule pressure, invasive species outcompete and replace local biota (*5*). Indeed, the spread of invaders is often facilitated by corridors, either natural (rivers, coastlines, ridges) or man-made (roads and railways). In this context, it is worth mentioning that all the plants considered in the South Carolina studies [Levey *et al.*; (*1*)] are aliens of concern in parts of the world [*Lantana camara* (*6*), *Rudbeckia hirta* (*7*), *Morella* (=*Myrica*) *cerifera* (*8*)]. Moreover, the Eastern Bluebird (*Sialia sialis*) that dispersed *Morella* seeds is also known to disperse seeds of the alien tree *Sapium sebiferum* in the eastern United States (*9*).

Presently, land managers are advised to build habitat corridors to reduce the effects of habitat fragmentation, but habitat barriers are also built to manage the spread of invasive species (*10*). It is ironic that habitat corridors do not always link the seemingly separate fields of conservation and invasion biology. Both habitat fragmentation and invasive species have resulted in the loss of large sections of biodiversity, and their combined impacts must be better understood. The modeling tools developed in the present study present a useful opportunity for developing a more integrated approach to the evaluation of corridors as a conservation management tool.

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References

1. P. A. Townsend, D. J. Levey, *Ecology* **86**, 466 (2005).
2. D. A. Saunders, R. J. Hobbs, Eds., *Nature Conservation 2: The Role of Corridors* (Surrey Beatty & Sons, Chipping Norton, Australia, 1991).
3. D. Simberloff, *Annu. Rev. Ecol. Syst.* **19**, 473 (1988).
4. D. M. Richardson, N. Allsopp, C. M. D'Antonio, S. J. Milton, M. Rejmánek, *Biol. Rev.* **75**, 65 (2000).
5. J. L. Lockwood, P. Cassey, T. Blackburn, *Trends Ecol. Evol.* **20**, 223 (2005).
6. See www.gisp.org.
7. J. S. Meidell, H. L. Oppenheimer, R. T. Bartlett, *Bishop Mus. Occ. Pap.* **49**, 17 (1997).
8. E. U. Zajac, *Monogr. Bot.* **40**, 1 (1974).
9. I. J. Renne, W. C. Barrow, L. A. J. Randall, W. C. Bridges, *Div. Distrib.* **8**, 285 (2002).
10. K. A. With, *Conserv. Biol.* **16**, 1192 (2002).

Response

PROCHEŞ *ET AL.* POINT OUT THAT CORRIDORS may increase the spread of exotic species. We agree that the function of corridors is blind to the geographic origin of species that use them.

The issue before conservation biologists and land managers, however, is not whether corridors are without costs, but whether they provide a net benefit in the maintenance of natural communities. In this context, it is important to keep in mind that the benefits of habitat corridors to native species have been clearly demonstrated, whereas their impact on the spread of exotic species is largely conjectural.

Rather than debating the potential drawbacks of corridors, scientists should focus attention on understanding how corridors function and which types of species are most likely to benefit from them. For example, because invasive species are excellent dispersers (by definition), corridors may not further increase their successful colonization of new habitat patches. On the other hand, many native species of conservation concern have limited dispersal abilities and therefore would be more likely to benefit from corridors.

Understanding corridors at a mechanistic level will better enable us to extrapolate their effects from well-studied species and small spatial scales to less-known species and landscape scales; our paper aimed toward this goal.

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TECHNICAL COMMENT ABSTRACTS

COMMENT ON "A Brief History of Seed Size"

Peter J. Grubb, David A. Coomes, Daniel J. Metcalfe

Moles *et al.* (Reports, 28 Jan. 2005, p. 576) suggested that larger plants have larger seeds because larger offspring offset the lower survivorship to adulthood inherent in longer juvenile periods. However, that view is not consistent with the wedge-shaped relationship between log seed size and log plant height. Most importantly, the range of feasible seed sizes increases dramatically with whole-plant size.

Full text at www.sciencemag.org/cgi/content/full/310/5749/783a

RESPONSE TO COMMENT ON "A Brief History of Seed Size"

Angela T. Moles, David D. Ackerly, Campbell O. Webb, John C. Tweddle, John B. Dickie, Mark Westoby

Mechanical constraints might prevent small plants from making very large seeds. However, data for 2589 species reveal an absence of large plants that make very small seeds. This cannot be explained by mechanical constraint. Coordination of life history traits provides a more plausible explanation for the overall shape of the relationship between seed mass and plant size.

Full text at www.sciencemag.org/cgi/content/full/310/5749/783b

Letters to the Editor

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